REMARKS

In the outstanding Office action, claims 1 to 20 were presented for examination. Claims 11, 12, 15, and 17 were withdrawn from further consideration. Claims 1-10, 13, 16 and 18-20 were rejected.

In this amendment applicant has amended each of claims 1-10, 13, 16 and 18-20 as well as each of withdrawn claims 11, 12, 15, and 17. Claim 14 has been cancelled, without prejudice. Thus, claims 1-10, 13, 16 and 18-20 are now pending for examination and claims 11, 12, 15, and 17 are believed eligible for rejoinder, as will be discussed in detail below. Accordingly, it is believed that the application is in condition for allowance.

Claim Amendments

Each of the claims has been corrected to overcome the objection raised with regard to use of a definite or an indefinite article.

Claim 1 has been amended, without narrowing, and by making explicit language that was inherent in the claim before amendment, so as to more particularly point out the invention claimed.

Claims 5, 15 and 20 have been amended to more particularly define the amino acid sequences recited and to correct the antecedent basis. Support for the amendment made can be found at page 10, line 30 to page 11, line 1.

Claim 8 has been amended to recite that the water content is maintained below 2 weight percent to prevent crystallization of the recombinant or synthetic gelatin for at least 7 years.

Claim 13 has been amended to recite lyophilizing the vaccine composition with sufficient drying to prevent crystallisation. Reference to "bi-modal or multi-modal gelatin" has been deleted.

Minor amendments have been made throughout the claims for readability, without narrowing or to make explicit language that was inherent in the respective claim before amendment.

Claim Rejections - 35 U.S.C. § 112 Second Paragraph

Claims 5 and 20, were rejected under 35 U.S.C. § 112 second paragraph for allegedly being indefinite with regard to the phrase "said gelatin".

Without acquiescing to the rejection, and to expedite prosecution, claims 5 and 20 have been amended to overcome the rejection by reciting that "said gelatin" is "said recombinant or synthetic gelatin."

Claims 5 and 20 have also been amended to avoid use of the phrase "essentially similar."

Reconsideration and withdrawal of the rejection of claims 5 and 20 for indefiniteness are respectfully requested.

Claim Rejections - 35 U.S.C. § 102(b) Alleged Anticipation

In the outstanding Office action, claims 1-10, 13, 16 and 18-20 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by International Publication No. WO 01/34801 ("the '801 publication" herein), "as evidenced by" U.S. Patent No. 6,685,940 ("the evidentiary reference '940" herein).

In reply, applicant respectfully submits that applicant's claim 1, as now amended, is patentably distinguished from the '801 publication, for reasons which will now be explained.

As is discussed at page 3 lines 16-25 of applicant's specification, the '801 publication suggests using recombinant gelatin polypeptides as vaccine stabilizers to avoid problems associated with the use in vaccines of gelatin derived from animal sources. However, the '801 publication does not appear to explicitly describe the production of a vaccine composition comprising recombinant gelatin as a stabilizer and appears to be unaware of the problems that can arise.

The '801 publication appears to describe that animal-derived gelatin can simply be replaced by recombinant gelatin as a stabilizer in vaccine compositions. See for example page 64, lines 19-20. However, the '801 publication does not appear to describe the surprising problems which can arise.

As explained in applicant's specification, for example at page 3, line 28 to page 4, line 12, a simple replacement of animal-derived gelatin in a vaccine composition by recombinant gelatin yields unsatisfactory results. For example, lyophilized vaccine compositions may be more difficult to produce and have a shorter shelf life than analogous compositions comprising animal-derived protein.

As described in applicant's specification, it was found that crystallization occurred in vaccine formulations when employing recombinant gelatin as a stabilizer, whereas such a problem had not been observed with animal-derived gelatin. Apparently owing to the heterogeneous nature of animal-derived gelatin, the problem of crystallization did not occur in previously known vaccine compositions. The absence of such heterogeneity from recombinant or synthetic gelatins is believed by applicant to explain the phenomenon of crystallization, although the claimed invention is not limited by this or any other theory.

Also, it was discovered by applicant that, surprisingly, a small amount of moisture could trigger crystallization of recombinant or synthetic gelatin, resulting in an unstable vaccine composition and a shortened shelf life. Accordingly, it was found that by reducing the water content of the vaccine composition, and preventing moisture from contacting it, the newly discovered problem of crystallization could be prevented.

Applicant's claim 1, as now amended, relates to a method for the preparation of a vaccine composition comprising recombinant or synthetic gelatin as a stabilizer. The claimed method comprises two steps: a first step of reducing the water content of the vaccine composition to be below 2 weight percent; and a second step of maintaining the water content below 2 weight percent for at least 2 years.

Applicant respectfully submits that the '801 publication does not disclose reducing the water content of a vaccine composition stabilized with a recombinant gelatin below 2 weight percent, as will now be explained.

The Office action argues that because the referenced '801 publication discloses, in claims 18- 19, a vaccine composition comprising a gelatin and antigen which composition is dry and is a powder, the lyophilization process of the reference results in dryness of the composition, the claimed water content below 2 weight percent has been met and the prevention of recombinant gelatin from crystallization is inherently achieved. Applicant respectfully disagrees.

"Dry" is a relative term as is apparent from the '801 publication itself. For example while claims 18 and 19 of the '801 publication recite that the claimed vaccine formulation is "dry", or "powdered", respectively, these claims can be compared with claim 17 which recites that the claimed vaccine formulation is liquid. Also, the '801 publication makes reference to two stages of drying in the lyophilization process

described at page 62, lines 30-32, a primary drying and a secondary drying. Thus, the product of primary drying, though "dry" retains some unspecified proportion of water which is to be removed by a secondary drying. Furthermore, there appears to be nothing in the disclosure of the '801 publication to contradict the possibility that the product of the secondary drying could have a water content in excess of 2 weight percent depending upon the drying conditions. Indeed the tests described at pages 14 and 15 of applicant's specification show that a two stage freeze-drying of a recombinant gelatine can yield a product having a water content of 2.4 weight percent.

To establish inherency, the extrinsic evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient. See *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999.)

For the reasons explained above, applicant believes that the water content of the recombinant gelatin stabilized vaccine composition disclosed in the '801 publication can vary, according to the drying conditions, is not described as being below 2 weight percent and is not inherently below 2 weight percent. Accordingly, applicant believes claim 1 is patentably distinguished from the '801 publication and is therefore allowable.

In summary, the '801 publication is silent on the problem of crystallisation of recombinant gelatine in vaccine compositions, on what causes recombinant gelatin crystallization and on how recombinant gelatin crystallization can be prevented. Specifically, the '801 publication does not describe the use of sufficient drying time during lyophilization to obtain a low enough water content to avoid crystallization.

Furthermore, applicant respectfully submits that the '801 publication does not disclose maintaining the water content of a vaccine composition stabilized with a recombinant gelatin below 2 weight percent for at least 2 years, as will now be explained.

In connection with applicant's claims 8 and 9, the Office action argues that the '801 publication teaches a kit and that the evidentiary reference '940 discloses that a lyophilized protein can be packaged in a vial in a kit. The Office action further argues that a kit inherently comprises a container and this container *should* prevent *any* leakage, therefore, the container is a *sufficiently* air or moisture tight container and that therefore, the reference teachings anticipate the claimed invention (emphasis added). The emphasized language implicitly acknowledges that the container could leak and might not be sufficiently air or moisture tight. Furthermore, the container could be opened during the lifetime of the vaccine composition, admitting moisture, and then closed again and stored causing any residual vaccine composition in the container to deteriorate.

Accordingly, applicant believes that even when it is considered in the light of the evidentiary reference '940 the '801 publication does not disclose, explicitly or inherently, the limitation in applicant's amended claim 1 of maintaining the water content of a vaccine composition stabilized with a recombinant gelatin below 2 weight percent for at least 2 years. It follows that amended claim 1 is patentably distinguished from the '801 publication and therefore allowable for this additional reason.

In the outstanding Office action, claims 1-10, 13, 16 and 18-20 were also rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by US 2003/0064074 ("the '074 publication" herein), as evidenced by U.S. Patent No. 6,685,940.

It appears to applicant that the disclosure of the '074 publication is similar to that of the '801 publication. Accordingly, applicant believes that amended claim 1 is patentably distinguished from the '074 publication, and therefore allowable, for the same reasons that amended claim 1 is believed to be patentably distinguished from the '801 publication.

Also, applicant believes that Claim 13, as now amended, is patentably distinguished from the '801 publication and the '074 publication, because neither the '801 publication nor the '074 publication discloses lyophilizing a recombinant gelatin containing vaccine composition for sufficient time to prevent crystallization of the recombinant gelatin, as is recited in amended claim 13, as has been explained above.

Amended claim 16 contains limitations similar to amended claim 1 and is accordingly believed patentably distinguished from the '801 publication for the same reasons as claim 1.

Dependent Claims

Claims 2-10 and 18-20 which depend either directly or indirectly from amended claim 1, incorporate all the limitations of claim 1 and therefore are believed allowable for at least the same reasons that amended claim 1 is believed allowable. Applicant believes that dependent claims 2-10 and 18-20 also are patentably distinguished from the art of record, and therefore allowable, by the additional limitations they recite.

For example, Claim 8 specifically recites that the water content is maintained below 2 weight percent to prevent crystallization of the recombinant or synthetic gelatin for at least 7 years, which is not remotely suggested by the '801 publication or any of the other art of record in this application.

The Office action refers to the disclosure on page 60 of the '801 publication, and alleges that the '801 publication further teaches that the lyophilized vaccine is stable for 24 months of storage. Applicant respectfully submits this statement is an incorrect characterization of the reference. The '801 publication actually states, at page 60, lines 36-37 that

> Lyophilized vaccines slowly deteriorate until, at around 12 to 24 months of storage, the vaccine formulation lacks sufficient titer to confer immunization.

Accordingly, applicant believes the '801 publication also does not disclose the additional subject matter recited in claim 8. Furthermore, applicant believes the '801 publication does not describe the making of an actual vaccine composition comprising a recombinant gelatin, does not describe keeping such a vaccine composition in a moisture-tight and/or air-tight container, does not mention the problem of crystallisation of gelatin and does not describe or suggest such a vaccine composition that is stable for at least 2 years

Rejoinder

Claims 11, 12, 15 and 17 as now amended recite limitations similar to the limitations which patentably distinguish amended claim 1 from the art of record. Accordingly, applicant believes claims 11, 12, 15 and 17 are eligible for rejoinder and rejoinder is respectfully requested.

Conclusion

In view of the above amendments and the discussion relating thereto, it is respectfully submitted that the instant application, as amended, is in condition for allowance. Favorable reconsideration and allowance are earnestly solicited. If for any reason the Examiner feels that consultation with applicant's representative would be helpful in the advancement of the prosecution, the Examiner is invited to contact the undersigned practitioner.

Respectfully submitted,

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